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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/623,577	07/22/2003	Raymond Pratt	109536.183	6543

24395 7590 06/07/2007

WILMER CUTLER PICKERING HALE AND DORR LLP
1875 PENNSYLVANIA AVE., NW
WASHINGTON, DC 20004

EXAMINER
ANDERSON, JAMES D

ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
06/07/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

michael.mathewson@wilmerhale.com
teresa.carvalho@wilmerhale.com
tina.dougal@wilmerhale.com

Office Action Summary	Application No.	Applicant(s)	
	10/623,577	PRATT, RAYMOND	
	Examiner	Art Unit	
	James D. Anderson	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36,37,39-43,45-52,54 and 55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36,37,39-43,45-52,54 and 55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

CLAIMS 36, 37, 39-43, 45-52 & 54-55 ARE PRESENTED FOR EXAMINATION

Continued Examination Under 37 CFR § 1.114

A request for continued examination under 37 CFR § 1.114, including the fee set forth in 37 CFR § 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR § 1.114, and the fee set forth in 37 CFR § 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR § 1.114. Applicant's submission filed on 5/17/2007 has been entered. Accordingly, claims 36, 42 and 48 are amended and claims 38, 44 and 53 are cancelled.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 36, 37, 39-40, 42, 43, 45-46, 48-52 and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ukai *et al.* (U.S. Patent No. 6,576,677; Issued June 10, 2003) (prior art of record).

Applicant's arguments have been fully considered but they fail to persuade the Examiner of an error in his determination of obviousness. Firstly, Applicant argues that the Ukai *et al.* formulations have an acidic pH, whereas the present claims recite a basic pH range. This is not persuasive because Ukai *et al.* disclose a pH range of 3 to 7, thus teaching a range that overlaps the instantly claimed ranges of 6.5 to 9 and 7 to 8.5. Secondly, Applicant argues that the Ukai *et*

al. reference suggests that optimization of the polyvinylpyrrolidone amounts would require increased amounts of polyvinylpyrrolidone rather than the "lower amounts" required by the instant claims. This is not persuasive because, as discussed in the previous Office Action and reiterated below, Ukai *et al.* explicitly teach a formulation comprising about 2% polyvinylpyrrolidone and further suggest that lower amounts may be added if the polyvinylpyrrolidone has a high molecular weight. Applicant concludes by asserting that the medicament species addressed by Applicant is in a different form than Ukai *et al.* This is not persuasive because the instant claims recite pharmaceutically acceptable salts of donepezil. Clearly, the donepezil hydrochloride recited in Ukai *et al.* is a pharmaceutically acceptable salt of donepezil. The rejection of the claims in maintained for the reasons of record and reiterated below.

Ukai *et al.* disclose liquid dosage formulations of donepezil hydrochloride comprising polyvinylpyrrolidone, 70% sorbitol, a pH-adjusting agent, preservatives, solvents, antioxidants, and flavoring agents (see especially cols. 6-8). It is further disclosed that the pH of the liquid formulations is usually 3 to 7 (col. 3, lines 8-9) and can be adjusted by addition of varying amounts of citric acid, thereby teaching the pH limitations of claims 36, 39, 42, 45, 48 and 54. The reference specifically discloses orally available liquid dosage formulations comprising: (i) 5 mg donepezil HCl (0.1% by weight); (ii) 4.8% by weight povidone K30 (polyvinylpyrrolidone with average M.W. of 40,000); (iii) 34% by weight 70% sorbitol; (iv) 0.2% by weight citric acid; (v) 0.1% by weight sodium benzoate; (vi) 0.02% by weight sodium bisulfite; and (vii) 0.3% by weight flavoring agent (col. 6, Table 4). The formulation disclosed in Table 4 does not contain a solvent (*e.g.* propylene glycol). However, an alternate formulation disclosed in the reference

comprises: (i) 0.1 % by weight donepezil HCl; (ii) 5.7 % by weight povidone K30; (iii) 41% by weight 70% sorbitol; (iv) 0.2% by weight citric acid; (v) 0.1% by weight methylparaben; (vi) 6.9% by weight propylene glycol; and (vii) 0.3% by weight flavoring agent (col. 8, Example 8). The formulation disclosed in Example 8 does not contain an antioxidant. The formulations disclosed in the reference differ from the instantly claimed formulations in the amount of polyvinylpyrrolidone present in the compositions.

However, Ukai *et al.* also disclose a formulation of donepezil (5 mg), polyvinylpyrrolidone (100 mg) in a total of 5 g solution (2% polyvinylpyrrolidone) (col. 4, Test 2). It is disclosed that the formulations reduce the unpleasant taste generally associated with donepezil liquid compositions (col. 4, Table 1 and col. 5) and when an antioxidant is present in the composition (sodium bisulfite), the formulations are stable for extended periods at elevated temperatures (col. 6, lines 26-30). Further, Ukai *et al.* disclose that "the larger the molecular weight of polyvinylpyrrolidone, the less the amount of it to be added, while the smaller, the more the amount to be added" (col. 2, lines 60-62). Thus, the patent teaches that the amount of polyvinylpyrrolidone present in the formulations is highly adjustable and that the ratio of basic medicament to polyvinylpyrrolidone differs depending on the molecular weight and cannot be determined in a "wholesale manner".

In the absence of a showing of unexpected results, the present formulations would have been *prima facie* obvious given the disclosure of Ukai *et al.* Formulations comprising the instantly claimed components in amounts encompassed by the present claims are specifically disclosed in the reference. The lower amount of polyvinylpyrrolidone (0.1 to 3%) in the instant claims compared to the 4.8 to 5.7% in the reference formulations would have been obvious given

the formulation disclosed in Test 2 (col. 4, lines 54-60) wherein only 2% polyvinylpyrrolidone and 0.1% donepezil were included in the composition. It is clear from the results in Table 2 that lower amounts of polyvinylpyrrolidone (*e.g.* 2%) demonstrated less numbing and bitter taste than higher amounts of polyvinylpyrrolidone (*e.g.* 10% and 14%). Thus, given these results and disclosure of formulations containing 2%, 4.8%, and 5.7% polyvinylpyrrolidone, and in the absence of a showing of unexpected results, no unobviousness is seen in the instantly claimed ranges of 0.5 to 2% and 0.1 to 3% polyvinylpyrrolidone. Further, Ukai *et al.* disclose that the larger the molecular weight of polyvinylpyrrolidone, the less the amount of it needs to be added, while the smaller the molecular weight, the more polyvinylpyrrolidone needs to be added (col. 2, lines 60-62). "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

The skilled artisan would be motivated to modify the formulation of Example 8 in the reference to include an antioxidant given the results of Test 4 (col. 6, lines 26-30) wherein a formulation containing sodium bisulfite ("Test Sample", Table 4) demonstrated better stability than a formulation wherein the antioxidant was omitted. Other antioxidants (*e.g.* sodium sulfite, ascorbic acid) are disclosed as being usable in the disclosed formulations (col. 3, line 40-45).

Accordingly, the instantly claimed formulations are deemed properly rejected as being obvious over Ukai *et al.*

Claims 41, 47, and 55 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Ukai *et al.* as applied to claims 36, 37, 39-40, 42, 43, 45-46, 48-52 and 54 above, and further in view of Sugimoto *et al.* (U.S. Patent No. 4,895,841; Issued January 3, 1990) (prior art of record).

Applicant does not present any arguments specific to this rejection. Rather, Applicant argues that because the claims are unobvious over Ukai *et al.*, the claims are also unobvious over Ukai *et al.* in view of Sugimoto *et al.* The Examiner has addressed Applicant's arguments traversing the rejection of the claims over Ukai *et al.* (see *supra*). In view of the above, the present rejection is maintained for the reasons of record and reiterated below.

Sugimoto *et al.* disclose that donepezil, its hydrochloride salt, and stereoisomers (see especially col. 34, Example 4 and col. 12, lines 30-48) are capable of inhibiting acetylcholinesterase and are thus effective for the treatment of various kinds of dementia and cerebrovascular diseases (col. 29, lines 52-65). The patentees further disclose effective dosages of from generally 0.1 to 300 mg and specifically 1 to 100 mg per day (col. 30, line 25). The compounds may be orally administered (col. 30, lines 10-11) and presented in a variety of dosage forms, such as injections, suppositories, sublingual tablets, tablets, and capsules (col. 30, lines 27-31).

In the absence of a showing of unexpected results commensurate in scope with the claims, it would have been *prima facie* obvious to formulate liquid compositions comprising the enantiomers of donepezil in the formulations disclosed in Ukai *et al.* The motivation to do is found in Sugimoto who disclose that donepezil, its hydrochloride salt, and stereoisomers are capable of inhibiting acetylcholinesterase and are thus effective for the treatment of various kinds of dementia and cerebrovascular diseases.

Accordingly, the claims are deemed properly rejected as being obvious over Ukai *et al.* in view of Sugimoto *et al.*

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James D. Anderson whose telephone number is 571-272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

James D. Anderson
Patent Examiner
AU 1614

May 30, 2007

Phyllis Spivack

PHYLLIS SPIVACK
PRIMARY EXAMINER 5/31/07